REMARKS

Claims 1-41, 46-53, 58-70, and 73-77 are pending in the application. Claims 22-41, 49-53, and 70, due to restriction requirement, are withdrawn from consideration, and claims 42-45, 54-57, 71, 72, and 77 were previously canceled. Claims 1-21 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of co-pending U.S. Serial No. 10/947,455, and over claims 1-24, 51-54, 66-80, and 82-85 of co-pending U.S. Serial No. 10/777,517. Claims 1-8, 11, 12, 15, 20, 21, 46-48, 58, 59, 62, 63, 66, and 73-76 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Siegel et al. (U.S. Patent No. 6,204,245; hereafter "Siegel"). Claims 10 and 62 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Siegel in view of The Merck Index monograph numbers 04972 and 03712. Claims 13, 14, 16-18, 64, 65, and 67-69 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Siegel in view of Linden et al. (*Am. J. Medicine* 107:595-605, 1999; hereafter "Linden"), Guenther (*J. Am. Acad. Dermatol.* 43:S36-S42, 2000), and Mitra (*Indian J. Dermatol. Venereologyand Leprology* 67:292-293, 2001). Lastly, claims 13, 14, 64, and 65 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Siegel in view of Ahmed (U.S. Patent No. 6,281,248) and The Merck Manual Section 4, Chapter 44, Asthma.

Rejections Based on Double Patenting

Claims 1-21 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of co-pending U.S. Serial No. 10/947,455, and over claims 1-24, 51-54, 66-80, and 82-85 of co-pending U.S. Serial No. 10/777,517. This is a provisional rejection, as the '455 and '517 applications have not yet issued as patents. Applicants wish to hold these rejections in abeyance until indications of allowable subject matter in this application have been received.

Rejections under 35 U.S.C. § 103(a)

Claims 1-8, 10-18, 15, 20, 21, 46-48, 58, 59, 62-69, and 73-76 stand rejected as being obvious over Siegel, either alone or in combination with one or more of The Merck Index monograph numbers 04972 and 03712, Linden, Guenther, Mitra, Ahmed, and The Merck Manual Section 4, Chapter 44. Applicants respectfully traverse this rejection.

The Office cites Siegel as providing the basis for the combination of an SSRI and a corticosteroid. The Office cites the additional references for teaching additional elements of the pending claims (i.e., infliximab, etanercept, retinoids, vitamin D analogs, psoralens, and beta receptor agonists).

Siegel teaches the combination of an immunosuppressive agent from a list of 14 different agents (e.g., glucocorticoid; column 3, lines 49-56) and an additional agent from a list of 29 agents (e.g., a selective serotonin reuptake inhibitor (SSRI), fluoxetine, paroxetine, and sertraline; column 3, line 58, to column 4, line 3) for the treatment of narcolepsy and cataplexy. Applicants submit that the Office has failed to provide a reason why one skilled in the art would choose the combination of an SSRI and a glucocorticoid from the 406 different combinations (14 x 29 = 406) disclosed by Siegel, and, for this reason, a *prima facie* case of obviousness has not been made.

The Supreme Court recently commented on the standard for obviousness rejections:

> Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to *identify a reason* that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. KSR Int'l Co. v. Teleflex Inc. 550 U.S. _____, 82 USPQ2d 1385 (2007) (emphasis added).

Applicants submit that the Office has not provided a reason why a person skilled in the art would arrive at the Applicants' invention in view of the large number of potential combinations disclosed in Siegel.

Moreover, as is described in greater detail below, Applicants have discovered that the combination of an SSRI and a corticosteroid has an unexpected, synergistic effect on decreasing proinflammatory cytokine secretion and production (see, Tables 15-22 of the specification). The Supreme Court's recent comments on *United States v. Adams* (383 U.S. 39 (1966)) in *KSR International Co. v. Teleflex Inc.* (550 U.S.____, 82 USPQ2d 1385 (2007), page 13) support a finding of nonobviousness in view of an unexpected result:

> The fact that the elements worked together in an unexpected and fruitful manner supported the conclusion that Adams's design was *not obvious* to those skilled in the art. (Emphasis added).

In addition, the USPTO's Examination Guidelines for Determining Obviousness Under 35 103 In View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* (Federal Register Vol. 72, No. 195, page 57534) instructs:

> [I]n the case of a claim to a combination, applicants may submit evidence or argument to demonstrate that:
> (1) one of ordinary skill in the art could not have combined the claimed elements by known methods (e.g., due to technological difficulties);
> (2) the elements in combination do not merely perform the function that each element performs separately; or
> (3) the results of the claimed combination were *unexpected.* (emphasis added).

The specification provides data (see, Tables 15-22) that demonstrate the unexpected effect of the combination of an SSRI and a corticosteroid on decreasing proinflammatory cytokine secretion and production. For example, data showing the synergistic effect of the combination of an SSRI and a corticosteroid on decreasing TNFα secretion is found in the specification: paroxetine and prednisolone (Table 15, page 84; 0.375 μM paroxetine + 0.025 μM prednisolone); fluoxetine and prednisolone (Table 16, page 84; 7.23 μM fluoxetine + 0.006 μM prednisolone); fluoxetine and budesonide

(Table 17, page 84; 0.009 μM fluoxetine + 0.009 μM budesonide); paroxetine and dexamethasone (Table 18, page 85; 3.0 μM paroxetine + 0.0063 μM dexamethasone); fluoxetine and dexamethasone (Table 19, page 85; 0.036 μM fluoxetine + 0.0024 μM dexamethasone); fluoxetine and prednisolone (Table 20, page 85; 1.80 μM fluoxetine + 0.0160 μM prednisolone); paroxetine and prednisolone (Table 21, page 86; 3.30 μM paroxetine + 0.016 μM prednisolone); and sertraline and prednisolone (Table 22, page 86; 4.0 μM sertraline + 0.0160 μM prednisolone). These data are also summarized in the enclosed Exhibit 1, where it is clearly shown that the combined effect of an SSRI with a corticosteroid results in an effect that is greater than the sum of the effects of the SSRI and corticosteroid when administered alone.

As none of the cited art references teach the synergistic effect of the combination of an SSRI and a corticosteroid on decreasing proinflammatory cytokine secretion or production, Applicants therefore, respectfully request that the rejections under 35 U.S.C. § 103(a) be withdrawn.

Lastly, Applicants further submit that the rejection of claims 13, 14, 16-18, 64, 65, and 67-69 over Siegel in view of Linden, Guenther, and Mitra is improper as Siegel is directed to a purpose entirely different from that of Linden, Guenther, and Mitra. As acknowledged by the Office (Office Action; page 15), M.P.E.P. § 2144.06 states:

> It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the *same purpose*, in order to form a third composition to be used for the *very same purpose*....[T]he idea of combining them flows logically from their having been individually taught in the prior art. *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). (Emphasis added).

As discussed above, Siegel is directed to compositions and methods for the treatment of *narcolepsy* and *cataplexy*. Linden, Guenther, and Mitra are each directed to the treatment of *psoriasis*. The Office provides no reasoning as to why one would combine the teachings of Siegel with those of Linden, Guenther, and

Mitra. Indeed, it would not have been obvious for one skilled in the art to combine the cited references as the Office proposes to arrive at the Applicants' invention. For this reason, the rejection of claims 13, 14, 16-18, 64, 65, and 67-69 over Siegel in view of Linden Guenther, and Mitra should be withdrawn.

For all the above reasons, Applicants respectfully request that the rejections under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

Applicants submit that the application is in condition for allowance, and such action is hereby requested.

Enclosed is a Petition to extend the period for replying to the Office Action for three months, to and including April 11, 2008, and a check in payment of the required extension fee. If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 4/10/08

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Exhibit 1

Support in Specification	SSRI	SSRI Dose	Corticosteroid	Corticosteroid Dose	% Decrease SSRI Alone	% Decrease Corticosteroid Alone	Expected % Decrease of Combination	Actual % Decrease of Combination
Table 15	paroxetine	0.375 μM	prednisolone	0.025 μM	1.4	16.5	17.9	**22.4**
Table 16	fluoxetine	7.23 μM	prednisolone	0.006 μM	29.6	7.0	36.6	**42.4**
Table 17	fluoxetine	0.009 μM	budesonide	0.009 μM	7.9	5.3	13.2	**43.6**
Table 18	paroxetine	3.0 μM	dexamethasone	0.0063 μM	9.9	26.7	36.6	**42.0**
Table 19	fluoxetine	0.036 μM	dexamethasone	0.0024 μM	22.7	0.25	23.0	**35.0**
Table 20	fluoxetine	1.80 μM	prednisolone	0.0160 μM	5.5	10.5	16.0	**19.4**
Table 21	paroxetine	3.30 μM	prednisolone	0.016 μM	29.1	12.9	42.0	**50.3**
Table 22	sertraline	4.0 μM	prednisolone	0.0160 μM	19.4	6.3	25.7	**29.0**